the Act, if they are applied to the marketing areas as proposed to be redefined, and, if not, what modifications of the provisions of the orders would be appropriate.

In addition to the proposed amendments listed in the hearing notices issued on September 19, and September 27, 1968, evidence will be received with respect to the proposed amendments, or to appropriate modifications thereof, listed below under Proposal No. 2. For the convenience of interested parties, all proposals to be considered at this hearing are listed below.

The proposed amendments, set forth below, have not received the approval of the Secretary of Agriculture.

Proposed by Dairymen's Cooperative Sales Association:

Proposal No. 1. Combine into one order the present Order 36 (Eastern Ohio-Western Pennsylvania) and Order 9 (Clarksburg, W. Va.), retaining for the merged order the present provisions of Order 36 and providing therein for a Class I price for plants in the Clarksburg area at the same level as that set forth in the current provisions of the Clarksburg order in § 1009.51(a).

Proposed by Fairmont Foods Company:

Proposal No. 2. Combine Order 5 (Tri-State) and Order 9 (Clarksburg, W. Va.) into one order, retaining for the merged order the present provisions of Order 5 with the following changes:

A. Amend § 1005.6 by adding a new paragraph to read as follows:

(c) "Clarksburg District" means all the territory within the boundaries of the following:

(1) West Virginia counties of Monongalia, Marion, and Harrison;

(2) Grafton Magisterial District in Taylor County, Philippi Magisterial District in Barbour County, Leadsville Magisterial District in Randolph County, the city of Buckhannon in Upshur County, the city of Weston in Lewis County, and the town of Kingwood in Preston County, all in the State of West Virginia.

B. Amend § 1005.51(a)(1) to read as follows:

(1) Add $1.55 for plants in the Charleston-Huntington District, $1.47 for plants in the Athens-Scioto District and $1.62 for plants in the Clarksburg District, plus 20 cents for each district.

C. Amend § 1005.51(a)(1) to add Clarksburg to the list of cities in West Virginia under this section.

D. Amend § 1005.72(a) as follows:

(a) The uniform price for producer milk at a pool plant shall be adjusted as follows:

(1) Except as provided in paragraph (b) of this section, reduced according to the location of the pool plant at the rates set forth in § 1005.53;

(2) Reduced an additional 8 cents at a pool plant at which the Athens-Scioto District Class I price is applicable; and

(3) Increased by 7 cents at a pool plant at which the Clarksburg District Class I price is applicable.

Proposed by the Dairy Division, Consumer and Marketing Service:

Proposal No. 3. Revise §§ 1009.51(b) and 1036.51(b) to read as follows:

(b) *Class II price.* The Class II price shall be the basic formula price for the month: *Provided,* That such Class II price shall not be more than the price computed pursuant to subparagraphs (1), (2), and (3) of this paragraph:

(1) Multiply by 4.2 the Chicago butter price;

(2) Multiply by 8.2 the weighted average of carlot prices per pound of nonfat dry milk solids, spray process, for human consumption, f.o.b. manufacturing plants in the Chicago area, as published for the period from the 26th day of the preceding month through the 25th day of the current month by the Department; and

(3) From the sum of the results arrived at under subparagraphs (1) and (2) of this paragraph subtract 48 cents, and round to the nearest cent.

Proposal No. 4. Make such changes as may be necessary to make the entire marketing agreements and the orders conform with any amendments thereto that may result from this hearing.

Copies of this notice of hearing and the orders may be procured from Market Administrators W. W. Hurwitz, 7503 Brookpark Road, Post Office Box 29066, Cleveland, Ohio 44129; and Charles T. McCleery, 19 Locust Street, Post Office Box 33, Gallipolis, Ohio 45631; or from the Hearing Clerk, Room 112-A, Administration Building, U.S. Department of Agriculture, Washington, D.C. 20250, or may be there inspected.

Signed at Washington, D.C., on November 6, 1968.

JOHN C. BLUM,
Deputy Administrator,
Regulatory Programs.

[F.R. Doc. 68-13585; Filed, Nov. 8, 1968; 8:48 a.m.]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 28]

CHERRY PIE

Further Extension of Time for Filing Comments on Proposed Standards of Identity and Quality

In the matter of establishing a definition and standard of identity and standard of quality for cherry pie:

The notice of proposed rule making in the above-identified matter published in the FEDERAL REGISTER of November 1, 1967 (32 F.R. 15116), provided that comments could be filed regarding the proposal within 90 days following its date of publication. Notice was given in the FEDERAL REGISTER of February 16, 1968 (33 F.R. 3076), that the time for filing comments in this matter was extended to March 29, 1968, and in the FEDERAL REGISTER of March 15, 1968 (33 F.R. 4587), that it was further extended to September 30, 1968.

The National Red Cherry Institute and two other trade organizations have requested further extension to give additional time for the Department of Food Science of Michigan State University to complete research work designed to provide a better way for determining the amount or weight of cherries in cherry pie. The Institute included with its request a report of the research work.

The Commissioner concludes that further extension is in the public interest; therefore, the time for filing comments in this matter is extended to September 30, 1969.

This action is taken pursuant to the provisions of the Federal Food, Drug, and Cosmetic Act (secs. 401, 701, 52 Stat. 1046, 1055, as amended 70 Stat. 919, 72 Stat. 948; 21 U.S.C. 341, 371) and under authority delegated to the Commissioner (21 CFR 2.120).

Dated: November 4, 1968.

HERBERT L. LEY, Jr.,
Commissioner of Food and Drugs.

[F.R. Doc. 68-13575; Filed, Nov. 8, 1968; 8:47 a.m.]

Public Health Service

[42 CFR Part 73]

BIOLOGICAL PRODUCTS

Additional Standards; Typhoid Vaccine and Limits of Potency

Notice is hereby given that the Director, National Institutes of Health, proposes to amend Part 73 of the Public Health Service Regulations by prescribing specific standards of safety, purity, and potency for Typhoid Vaccine, and by prescribing the required potency for Typhoid Vaccine and Tetanus Immune Globulin (Human).

Inquiries may be addressed, and data, views, and arguments may be presented by interested parties, in writing, in triplicate, to the Director, National Institutes of Health, Public Health Service, 9000 Rockville Pike, Bethesda, Md. 20014. All relevant material received not later than 30 days after publication of this notice in the FEDERAL REGISTER will be considered.

Notice is also given that it is proposed to make any amendments that are adopted effective 60 days after publication in the FEDERAL REGISTER.

1. Amend the table of contents by adding the following:

ADDITIONAL STANDARDS: TYPHOID VACCINE

73.410 Proper name and definition.
73.411 U.S. Standard preparations.
73.412 Production of Typhoid Vaccine.
73.413 Potency test.
73.414 General requirements.
73.415 Equivalent methods.

2. Add the following immediately after § 73.406:

ADDITIONAL STANDARDS: TYPHOID VACCINE

§ 73.410 Proper name and definition.

The proper name of this product shall be Typhoid Vaccine which shall be an aqueous or dried preparation of killed *Salmonella typhosa* bacteria.

§ 73.411 U.S. Standard preparations.

(a) The U.S. Standard Typhoid Vaccine shall be used for determining the potency of Typhoid Vaccine.

(b) The U.S. Opacity Standard shall be used in estimating the bacterial content of the challenge culture.

§ 73.412 Production of Typhoid Vaccine.

(a) *Strain of bacteria.* Strain Ty 2 of *Salmonella typhosa* shall be used in the manufacture of Typhoid Vaccine.

(b) *Propagation of bacteria.* The culture medium for propagation of *S. typhosa* shall not contain ingredients known to be capable of producing allergenic effects in human subjects. The harvested bacteria shall be free of extraneous bacteria, fungi and yeasts, as demonstrated by microscopic examination and cultural methods.

(c) *Bacterial content.* (1) The number of bacteria in the concentrate of harvested bacteria shall be estimated not later than 2 weeks after harvest and before any treatment capable of altering the opacity of the bacterial concentrate.

(2) The number of *S. typhosa* bacteria in the vaccine shall not exceed 10^9 per ml.

(d) *Nitrogen content.* The total nitrogen content of the vaccine shall not exceed 0.035 mg./ml. for nonextracted bacteria preparations and shall not exceed 0.023 mg./ml. for acetone-extracted bacteria preparations.

(e) *Preservative.* Aqueous vaccine and the solution for reconstitution supplied with dried vaccine shall contain a preservative. Dried vaccine shall not contain a preservative.

§ 73.413 Potency test.

The number of potency units per milliliter shall be estimated for each lot of vaccine from the results of simultaneous mouse protection tests of the vaccine under test and of the U.S. Standard Typhoid Vaccine. The test shall be performed as follows:

(a) *Mice.* Healthy mice shall be used, all from a single strain and of the same sex, or an equal number of each sex in each group, with individual weights between 13 and 16 grams. A system of randomization shall be used to distribute the mice into the groups, with respect to shelf position and to determine the order of challenge. There shall be at least three groups consisting of no less than 16 mice each, for each vaccine. In addition, there shall be at least four groups consisting of no less than 10 mice each, for control purposes; one group for the challenge dose and three groups for titrating the virulence of the challenge dose.

(b) *Inoculation of vaccine.* (1) Serial dilutions, no greater than 5-fold, of the vaccine to be tested and of the standard vaccine shall be made in saline (0.85 percent sodium chloride solution). The mid-dilution of each vaccine shall contain that amount of vaccine which will afford protection to approximately 50 percent of the mice. Each mouse in each group for inoculation shall be injected intraperitoneally with 0.5 ml. of the appropriate dilution.

(2) The interval between vaccination and challenge shall be no less than 7 days nor more than 14 days. At least 87.5 percent of the mice in each group shall survive the period between inoculation and the challenge and each mouse challenged shall appear healthy.

(c) *The challenge.* (1) The challenge culture of Strain Ty 2 of *S. typhosa* for each test shall be taken from a batch of cultures maintained by a method, such as freeze-drying, that retains constancy of virulence.

(2) The challenge and virulence titration doses shall be prepared as follows: The bacteria shall be harvested from a 5- to 6-hour culture grown at 36°±1° C. on a nutrient agar medium which shall have been seeded from a 16- to 20-hour culture grown at 36°±1° C. on a nutrient agar medium, and the harvested bacteria then shall be uniformly suspended in saline. The suspension, freed from agar particles and clumps of bacteria and adjusted to an opacity of 10 units, shall be diluted in saline by tenfold increments. The suspensions for the challenge and virulence titration doses shall be put into a sterile gastric mucin preparation. The challenge suspension shall be prepared from whichever bacterial dilution provides about 1,000 colony forming units for an 0.5 ml. challenge dose. The virulence titration suspensions shall be 10^3, 10^4, and 10^5 dilutions respectively of the challenge suspension.

(3) Each mouse inoculated with vaccine shall be injected intraperitoneally with an 0.5 ml. dose of the challenge suspension. Each mouse in the four groups of control mice shall be injected intraperitoneally with an 0.5 ml. dose of the challenge suspension and its three dilutions, respectively. The challenge dose control mice shall be injected last. The interval between removal of the bacteria from the culture medium and the injection of the last mouse shall not exceed 2½ hours.

(d) *Recording the results.* The mice shall be observed daily for 3 days. A record shall be maintained of the number of mice that die. A record of the number of mice that survive shall be made at the end of the observation period.

(e) *Validity of the test.* The test is valid provided: (1) The ED_{50} of the vaccine under test and the Standard Vaccine is between the largest and smallest doses inoculated into the mice; (2) the limits of one standard deviation of the ED_{50} of each vaccine fall within the range of 61 percent to 163 percent; (3) a graded protective response is obtained in relation to the vaccine dilutions; (4) the dose response curves of the vaccine under test and the standard vaccine are parallel; (5) the challenge dose contains approximately 1,000 colony forming units; and (6) the LD_{50} of the challenge dose contains no more than 10 colony forming units.

(f) *Estimate of the potency.* The ED_{50} of each vaccine shall be calculated by a method that provides an estimate of the standard deviation. The protective unit value per milliliter of the vaccine under test shall be calculated in terms of the unit value of the standard vaccine.

(g) *Potency requirements.* The vaccine shall have a potency of eight units per milliliter. Variations in potency unit estimates are acceptable provided no estimate is less than 5.0 units per milliliter.

§ 73.414 General requirements.

(a) *Dose.* These standards are based on a human adult dose of 0.5 ml. for a single injection and a total immunizing dose of two injections of 0.5 ml. given at appropriate intervals.

(b) *Labeling.* In addition to the items required by other applicable labeling provisions of this part, the package label shall state that the vaccine contains eight units per milliliter.

(c) *Samples; protocols; official release.* For each lot of vaccine, the following material shall be submitted to the Director, Division of Biologics Standards, National Institutes of Health, Bethesda, Md. 20014:

(1) A sample of no less than 40 ml. of the product distributed in no less than four containers.

(2) A protocol which consists of a summary of the history of manufacture of each lot including all results of each test for which test results are requested by the Director, Division of Biologics Standards.

Typhoid Vaccine shall not be issued by by the manufacturer until notification of official release is received from the Director, Division of Biologics Standards, for each filling of dried vaccine and for each lot of aqueous bulk vaccine

§ 73.415 Equivalent methods.

Modification of any particular manufacturing method or process or the conditions under which it is conducted as set forth in the additional standards relating to Typhoid Vaccine, shall be permitted whenever the manufacturer presents evidence that demonstrates the modification will provide assurances of the safety, purity, and potency of the vaccine that are equal to or greater than the assurances provided by such standards, and the Director, National Institutes of Health, so finds and makes such finding a matter of official record.

3. Amend § 73.82 to include potency limits for Tetanus Immune Serum Globulin (Human) and for Typhoid Vaccine and revise that section to read as follows: